(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 July 2005 (07.07.2005)

PCT

(10) International Publication Number
WO 2005/061453 A1

(51) International Patent Classification[7]: C07D 207/06, 211/22, 211/46, 207/12, 207/08, 211/18, 211/38, 207/10, 207/46, 211/94, A61K 31/445, A61P 35/00

(21) International Application Number:
PCT/GB2004/005390

(22) International Filing Date:
22 December 2004 (22.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

0329820.5	23 December 2003 (23.12.2003)	GB
0330011.8	24 December 2003 (24.12.2003)	GB

(71) Applicant *(for all designated States except US)*: **SCHOOL OF PHARMACY, UNIVERSITY OF LONDON** [GB/GB]; 29-39 Brunswick Square, London WC1N 1AX (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **PATTERSON, Laurence, Hylton** [GB/GB]; School Of Pharmacy, University Of London, 29-39 Brunswick Square, London WC1N 1AX (GB). **PORS, Klaus** [DK/GB]; School of Pharmacy, University of London, 29-39 Brunswick Square, London WC1N 1AX (GB). **TEESDALE-SPITTLE, Paul, Henry** [GB/NZ]; School of Biological Sciences, Te Kura Matauranga Koiora, Victoria University of Wellington, P.O.Box 600, Wellington (NZ).

(74) Agent: **GILL JENNINGS & EVERY**; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB).

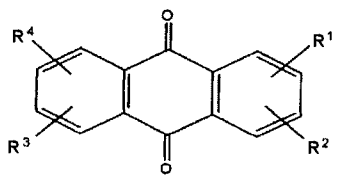
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

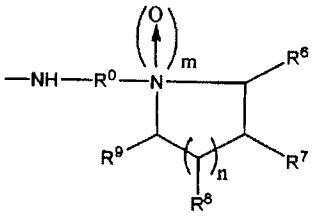
Published:
— *with international search report*

[Continued on next page]

(54) Title: ANTHARQUINONE COMPOUNDS AS ANTI CANCER COMPOUNDS



(I)



(II)

(57) Abstract: Anthraquinone compounds of the general formula (I) or a salt thereof (Formula I) in which R^1 to R^4 are each selected from the group consisting of H, C_{1-4} alkyl, X^1, $-NHR^0N(R^5)_2$ in which R^0 is a C_{1-12} alkanediyl and each R^5 is H or optionally substituted C_{1-4} alkyl, and a group of formula (II) in which at least one of R^6,R^7 and R^8 is selected from X^2 , and X^2 substituted C_{1-4} alkyl and any others are H or C_{1-4} alkyl; R^9 is selected from H, C_{1-4} alkyl, X^2 and X^2 substituted C_{1-4} alkyl; m is 0 or 1; n is 1 or 2; X^1 is a halogen atom, a hydroxyl group, a C_{1-6} alkoxyl group, an aryloxy group or an acyloxy group; and X^2 is a halogen atom, a hydroxyl group, a C_{1-6} alkoxyl group, an aryloxy group or an acyloxy group; provided that at least one of R^1 to R^4 is a group of formula (II). The N-oxides are useful prodrugs which are selectively bioreduced in hypoxic tumours to the corresponding cyclic amine derivatives. The amine compounds are cytotoxic and may be used as alkylating agents having topoisomerase II inhibiting activities in cancer therapy.

WO 2005/061453 A1

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.